Paper No. 35

THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

_____

Ex parte MYRON E. ESSEX,
TUN-HOU LEE,
WOAN-RUCH LEE
and
CHUN-NAN LEE

_____

Appeal No. 95-2419
Application 07/850,770[1]

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ON BRIEF

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Before WINTERS, WILLIAM F. SMITH and ROBINSON, Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. §134 from the final rejection of claims 1 through 14. As clarified at page 2 of the Supplemental Examiner's Answer (Paper No. 31, August 27, 1998), claims 1 through 10, 13 and 14 are now allowed. This leaves claims

[1] Application for patent filed March 13, 1992.

11 and 12 for our consideration. Claims 11 and 12 as well as allowed claim 1 from which these claims depend read as follows:

1. A composition comprising a mutant recombinant human immunodeficiency virus type 1 (HIV-1) envelope glycoprotein which is mutated in its primary amino acid sequence with respect to a wild type HIV-1 envelope glycoprotein, said mutant glycoprotein including two or more N-linked carbohydrate consensus amino acid sequence mutations so as to effect partial deglycosylation, said mutation being positioned between the C terminus of gp120 and the Cys at the N-terminal side of the gp120 cysteine loop containing the third hypervariable sequence (V3), said Cys being approximately at amino acid position 296, said mutant glycloprotein being sufficiently deglycosylated such that the total molecular mass of the mutant gp120 component is less than 90% of the corresponding fully glycosylated wild type gp120 component, said mutant glycoprotein being effective, when present as a component of a complete HIV virion, to enable viral infectivity.

11. A vaccine for use in protection of a human against infection with HIV-1, said vaccine comprising the mutant glycoprotein composition of claim 1.

12. A vaccine for use in treatment of a human infected with HIV-1, said vaccine comprising the mutant glycoprotein composition of claim 1.

The documents relied upon by the examiner as of the time of the Supplemental Examiner's Answer are:

Koff et al. (Koff), “Development and Testing of AIDS Vaccines,” Science, Vol. 341, pp. 426-32 (July 1988).

Schild et al. (Schild), “Modern Vaccines,” The Lancet, Vol. 335, pp. 1081-84, May 1990).

Flier et al. (Flier), “Vaccines Against Human Immunodeficiency Virus-Progress and Prospects,” The New England Journal of Medicine, Vol. 329, No. 19, pp. 1400-05 (Nov. 1993).

Cohen, “Jitters Jeopardize AIDS Vaccine Trials,” Science, Vol. 262, pp. 980-81 (Nov. 1993).

Greene, “AIDS and the Immune System, Scientific American, pp. 99-105 (Sept. 1993).

Brown, AIDS Vaccine Trials Viewed With Caution,” The Washington Post Newspaper (June 10, 1993).

Three documents of record which this merits panel discusses are:

Dirckx et al. (Dirckx), “Mutation of conserved N-glycosylation sites around the CD-4 binding site of human immunodeficiency virus type 1 GP120 affects viral infectivity,” Virus Research, Vol. 18, pp. 9-20 (1990).

Bolmstedt, et al., (Bolmstedt), “Effects of mutations in glycosylation sites and disulphide bonds on processing, CD4-binding and fusion activity of human immunodeficiency virus envelope glycoproteins,” Journal of General Virology, Vol. 72, pp. 1269-77 (1991).

Lee et al. (Lee), “Non-random distribution of gp120 N-linked glycosylation sites important for infectivity of human immunodeficiency virus type 1,” Proc. Natl. Acad. Sci., USA, Vol. 89, pp. 2213-17 (Mar. 1992).

The only rejection remaining in the appeal is that of claims 11 and 12 under 35 U.S.C. § 112, first paragraph (enablement). See pages 4-8 of the Supplemental Examiner's Answer. We affirm. In addition, we raise other issues which the examiner should consider upon return of the application.

DISCUSSION

By way of background, we refer to the paragraph bridging pages 2-3 of the supporting specification where appellants explain the basis of the present invention:

> We have discovered that selectively deglycosylated HIV-1 envelope proteins retain their ability to support viral infectivity, implying that they generally retain the native envelope conformation. We also noted that the envelope protein of the related simian virus for African green monkeys (SIV_{AGM}), which is not pathogenic to its natural host, has fewer N-linked glycosylation sites, particularly in the C-terminal portion of the surface envelope protein analogous to gp120. Without wishing to bind ourselves to a specific detailed molecular explanation, we propose that a selectively deglycosylated HIV-1 envelope protein is more effective in eliciting a protective immune response in people. Glycosylation serves to reduce or prevent immunological recognition of envelope protein domains. Selective deglycosylation enables an immune response to these domains and improves the opportunity for a protective immune response. Deglycosylation which produces substantial conformational changes (as determined by loss of infectivity) should be avoided.

Allowed claim 1 is directed to selectively deglycosylated HIV-1 envelope proteins as described in this paragraph.[2]

As seen from claims 11 and 12, these claims require more than claim 1, i.e., the claims are directed to a "vaccine." As explained on pages 4-8 of the Supplemental Examiner's Answer, the examiner's position is that one skilled in the art at the time of the present invention would have reasonably doubted whether the selectively deglycosylated HIV-1 envelope proteins set forth in claim 1 on appeal would function as a "vaccine." We agree that the facts of record support the examiner's conclusion.

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[2] The examiner has incorrectly stated at page 2 of the supplemental examiner's answer that claim 1 was amended on August 8, 1994 to recite three sentences. While the appendix to the Appeal Brief filed on that date contained an incorrect copy of claim 1, the record copy of the claim is properly written as a single sentence.

We understand that it is incumbent upon the Patent and Trademark Office (PTO) to explain why one skilled in the art would reasonably doubt the objective truth of the enabling statement contained in a supporting specification. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971). Here, there are no portions of the specification which are particularly helpful in providing enablement for the vaccine aspect of the present invention. As seen, for example, at page 8 of the specification, the selectively deglycosylated HIV-1 envelope proteins of the present invention are only viewed as "candidates" for vaccines. As explained at page 19, lines 9-19, of the supporting specification:

> Candidate vaccine gp120 molecules should generally possess the following properties: 1) they should be partially deglycosylated in the C-terminal portion of the molecule (defined above) to a sufficient extent to permit immune recognition of this portion of the molecule; and 2) a sufficient amount of the wild type conformation of the molecular should be retained such that the mutant virus substantially retains infectivity. A recombinant gp120 molecule which satisfies both of these criteria is likely to elicit a protective immune response to reduce viral infectivity.

As seen, partially deglycosylated proteins according to the present invention which meet these two criteria are only considered to be "candidates" for vaccine purposes.

Other relevant information in the supporting specification in regard to the vaccine aspect of the present invention is set forth at page 22, lines 22-30, as follows:

> The mutant envelope protein may be formulated into vaccines according to standard procedures known to those in the field. For example, procedures currently used to make wild-type envelope protein vaccines (e.g.,

> Microgenysys gp160 vaccine) can be used to make vaccines with the selectively deglycosylated envelope protein. Various modifications such as adjuvants and other viral or toxin components known for such vaccines or immunotherapeutics may be incorporated with the mutants.

It does not appear from this record that either appellants or the examiner have determined whether the referenced composition "Microgenysys gp160 vaccine" has been shown to be functional as a vaccine.

As set forth in Genentech Inc. v. Novo Nordisk A/s, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997):

> Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966)(stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

This application was filed on March 13, 1992. Instructive in considering the issue raised in this appeal is the decision in In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (footnote omitted) where the court agreed with the PTO that a vaccine "must by definition trigger an immunoprotective response in the host vaccinated; mere antigenic response is not enough." Keeping in mind that Wright was decided in 1993, after the effective filing date of this application, the court went on to state, Wright at 1563,

27 USPQ2d at 1514 (emphasis added): "The examiner made reference to the difficulty that the scientific community is having in developing generally successful AIDS virus vaccines merely to illustrate that the art is not even today as predictable as Wright has suggested that it was back 1983."

Appellants acknowledge at page 11 of the "Revised Brief" (Paper No. 22, August 11, 1994) that the claims stand rejected under 35 U.S.C. § 112, first paragraph (enablement). However, the arguments presented on pages 11-21 of that Revised Brief are directed to a now dropped companion rejection under 35 U.S.C. § 101 (utility). Nor does the Reply Brief (Paper No. 24, December 27, 1994) present any arguments directed to the enablement rejection. Suffice it to say that appellants have not presented any evidence that establishes that one skilled in the art would reasonably have expected that the selectively deglycosylated HIV-1 envelope proteins of the present invention would function as vaccines as required by claims 11 and 12 on appeal.

The rejection under 35 U.S.C. § 112, first paragraph (enablement) is affirmed.

OTHER ISSUES

We first direct attention to Lee. This reference was co-authored by several of the co-inventors of this application and describes the present invention. Based upon its publication date of March 1992, its prior art status is unclear. Be that as it may, it is of interest for its disclosure in the concluding paragraph which reads as follows:

> The findings of the present study suggest that consensus N-linked glycosylation sites that are important for viral infectivity are not randomly distributed in the gp120 molecule. Bolmstedt et al. (27) reported that the removal of N-linked glycosylation sites represented by our mutants 406 and 463 from the envelope recombinant proteins expressed by a vaccine expression vector did not affect CD4 receptor binding or syncytium formation (27). Their results are compatible with our findings that CD4-positive SupT1 cells were readily infected by our mutants 406 and 463, and support our hypothesis that the N-linked glycosylation sites located in the carboxyl-terminal half of gp120 are more dispensable for viral infectivity that those located in the amino-terminal half.

The Bolmstedt reference cited in Lee is of record. According to the record copy of the document, Bolmstedt was published in 1991. Thus, it appears to be legally available prior art on this record. Lee indicates that Bolmstedt "reported that the removal of N-linked glycosylation sites represented by our mutants 406 and 463 . . . did not effect CD4 receptor binding or syncytium formation." We point out that the allowed claims pending in this application encompass proteins "in which at least one of the N-linked glycosylation sequences corresponding to . . . 406 and 463" has been deglycosylated.
See claim 10 on appeal.

Upon return of the application, appellants and the examiner should take a step back and reassess the patentability of the allowed claims on appeal in light of the disclosure of Bolmstedt. The examiner should make sure that the record accurately reflects the outcome of that consideration.

We also point out that appellants filed a Supplemental Information Disclosure Statement on July 2, 1993 (Paper No. 14) citing Dirckx. It does not appear that the examiner has considered that paper. Since Dirckx is concerned with mutation of conserved N-glycosylation sites around the CD4-binding site of HIV-1 gp120, it may be relevant in determining the patentability of the claims pending in this application.

Again, upon return of the application, the appellants and the examiner should consider Dirckx and determine what effect, if any, it has on the patentability of the claims pending in the application. The examiner should also ensure that the record properly reflects the outcome of that determination.

The decision of the examiner is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Sherman D. Winters)
Administrative Patent Judge)
)
)
William F. Smith) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND
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